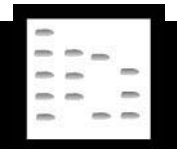
OCCUPATIONAL HYGIENE: GAS CHROMATOGRAPHY



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Introduction

Industrial or occupational hygiene has been defined as the anticipation, recognition, evaluation and control of environmental factors or stresses arising in or from the workplace that may cause sickness, impaired health or significant discomfort. The factors causing stress encountered in the workplace are typically divided into 'physical' and 'chemical', although, increasingly, a biological component has been recognized as, for example, with infectious diseases.

Chemicals can occur as gases, vapours and mists and as solids in the form of dusts and fumes. Their hazard potential is related to their ability to react with or be absorbed by the skin or lungs. The physiological response to exposure is related to its frequency, duration and severity, the route of exposure, and the chemical make-up of the substance, as well as factors relating to individual susceptibility. Gases and vapours can cause problems in the lungs by irritation, or can be absorbed into the bloodstream to cause problems elsewhere in the body. While such absorption is most likely in the lungs, substantial uptake of vapour is also possible through the skin. Liquids and solids also may be absorbed through the skin with local irritation or systemic effects, while aerosols can be deposited in various regions of the pulmonary system. In the lungs, certain dusts cause problems associated with their physical characteristics, while others are soluble and may be absorbed. Very fine particles may also enter the body and be transported elsewhere. Liquid droplets may cause irritation or be absorbed. Absorption of any chemical into the body may cause acute or chronic health effects in organs or tissues distant from the site of absorption. The most important classes of chemicals are the permanent gases, organic chemicals, inorganic acids and the heavy metals. Exposure limits for these chemicals are published by government and other agencies.

Monitoring of the environment is required to determine the nature and quantity of chemicals present, and also to evaluate the effectiveness of control measures. Monitoring is typically carried out through sampling, either of the air being breathed, or of surfaces which the skin or clothing may contact, or of the workers themselves through analysis of breath, blood or urine. Protocols have been established to standardize the methods of sampling and analysis. These methods are generally available, although they are often updated to meet the changing needs of hygiene investigations so that it is important to maintain a current awareness of the literature. Gas chromatography (GC) is one of a number of techniques used in the analysis of samples. It is used to separate the hazardous chemicals one from another, or from the matrix in which they are presented for analysis. GC is most often a laboratory analytical tool, but field-portable units are also available.

Factors in the Selection of Sampling and Analysis Methods

The ideal method would be specific, sensitive, and free from interference. In addition, it would provide real-time continuous output as well as time-integrated results. Finally, it would be simple and cheap to operate. It is rarely possible to satisfy all these criteria in currently available technology and compromise is often necessary.

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Air Sampling

There is substantial variation of hazardous chemical concentration in both space and time. To obtain accurate information concerning the airborne dose to the worker, it is necessary to sample air from the 'breathing zone'. Personal monitors therefore require an inlet port or sensor close to the face. Temporal variability can be covered by taking a time-integrated sample. Regulated concentration limits normally are expressed in terms of 8-h (work-shift) averages, although short-term limits are also employed for compounds with more acute toxicity. The time period for short-term averaging is typically 15 min in the USA, although other periods (e.g. 30 min) may be in use elsewhere. In addition, some regulations call for ceiling limits that cannot be exceeded under any circumstances. Although time periods for ceiling limit determinations are not stated, implying an instantaneous warning, in practice all monitoring equipment involves some time lapse. Equipment used for short-term sampling is often used to monitor ceiling values.

The simplest method for taking an air sample is to trap the air in an inert container. The air can be analysed either in the laboratory or in a field-portable gas chromatograph, by direct injection using a gas-tight syringe or gas sampling loop. Alternatively the chemical content can be concentrated by secondary trapping using a sorbent-filled or cryogenically cooled trap, and then released by rapid heating. The containers used include glass syringes or bottles, bags made of various polymers (e.g. Tedlar®, Teflon®, Mylar®, Saran®) or metal containers (stainless steel that has been electropolished, treated by the SUMMA® process or lined with fused silica). However, all such containers are bulky, even though smaller canisters have been manufactured recently to hold 200–500 mL of air and which can be worn on a belt or harness. There are issues of sample stability with whole-air samples. For example, many aromatic compounds are not stable in Tedlar bags over periods greater than 24 h, and their stability depends on the type of fitting used, with polypropylene providing greater stability than stainless steel. 1,3-Butadiene, on the other hand, is very stable in Tedlar bags, while dimethylformamide disappears very rapidly. Sulfur compounds are more stable in fused-silica lined canisters than in polished stainless steel. Tedlar bags should probably not be re-used as their integrity may be compromised, although they frequently are in practice. The expense of canisters ensures multiple re-use although carry-over to future samples is an issue when working from high concentrations to low, and contamination with oil mist renders a canister useless. There are also issues of sample recovery, due to photochemical reaction in transparent bags, or through moisture condensation on the interior of canisters.

The widespread development of sampling equipment to meet the combined needs of being lightweight, unobtrusive and carried by the worker, and of being able to provide time-weighted average results, has led to a simple method for a wide range of gases and vapours using a battery-operated pump to pull air through a tube filled with a sorbent (**Figures 1** and **2**). Changing the type or quantity of sorbent extends the range of vapours that can be collected. Another advantage is adjustable flow rate that can be raised to obtain sufficient sample to exceed detection limits at low concentrations or lowered to reduce the sample so that breakthrough does not occur at high concentrations.

Sorbents generally can be classified as being of two types: those that react with the chemical of interest and those that use adsorption to collect airborne vapour molecules. The former type is preferred for gases that are not readily condensed at room temperatures, for chemicals that are unstable or reactive, or where the reaction product can be detected with a better sensitivity. Some examples are reaction of aldehydes to stable hydrazone derivatives with analysis by GC or high performance liquid chromatography (HPLC), and the reaction of ethylene oxide with hydrobromic acid to form bromoethanol, which gives a good response with an electron-capture detector.

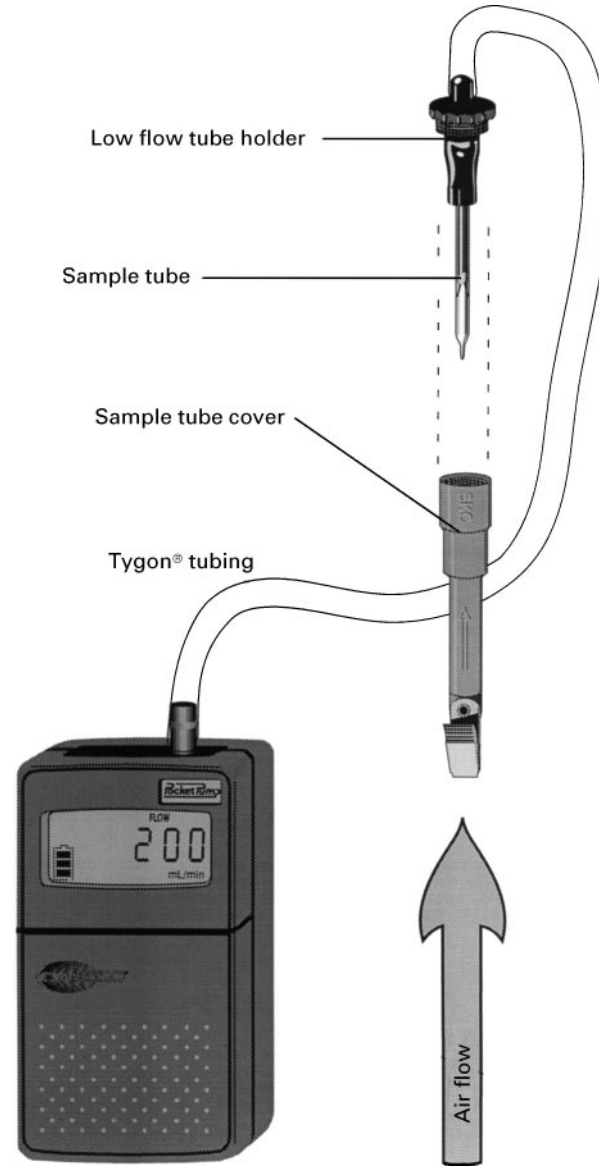

Figure 1 Typical personal air sampling train comprising sorbent tube and air-mover (pump). This is the commonest method of sampling worker exposure to hazardous gases and vapours.

The second type of sorbent, using microporous materials with high surface area, is more common. Activated carbons can have surface areas as high as $1000\ m^2\ g^{-1}$ or more, with a network of large pores

Figure 2 Personal air sampling train attached to a worker.

Figure 3 Diffusive sampler attached to a worker. This method is more acceptable to workers but the uptake rate varies from chemical to chemical and cannot be altered by field hygienists.

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leading to successively smaller pores with diameters in the nanometre range. Molecules that enter this region are affected by forces extending from the pore walls and from other molecules held in close proximity to them. Adsorption is strong and essentially complete at the low concentrations encountered in the air. Transport from the air stream to the sorbent is by molecular diffusion, and both diffusion and adsorption are relatively rapid. Thus only a small quantity of sorbent is required (as little as 100 mg) for effective removal of molecules from the air. The adsorbed chemicals are liberated from the charcoal after sampling by application of a polar solvent, commonly carbon disulfide.

Other sorbents are used routinely for particular applications. Many of these are the same polymeric resin materials used in chromatographic column packings. The range of sorbents is large, and complicated by the number of trade names used (e.g. Porapak® N or Q, Chromosorb® 102, 104 or 106, Amberlite® XAD-2, XAD-4 or XAD-7, or Tenax® TA or GR). One specific use for these sorbents is in thermal desorption, where the application of heat rather than a solvent is used to remove the collected chemicals. Graphitized carbon blacks are also used in this application.

An alternative to the use of pumps is to allow the molecules of the chemical being sampled simply to diffuse to the sorbent surface (**Figure 3**). Several styles of diffusive sampler are available, some of which develop colour reactions for on-site analysis, and others which contain the same types of sorbent used in the pumped tubes, and which are analysed in a similar manner.

Semi-volatile chemicals are normally sampled using a filter prior to the sorbent tube. A range of filters is available, including glass or quartz fibre, cellulose ester and polymeric membranes. The filter is extracted with a solvent, which may be the same as that used for the sorbent. This same arrangement is used where mists of volatile components are encountered.

Biological Sampling

Many occupational hygiene methods involve the analysis of breath, urine or blood samples. GC analysis may involve the chemical of interest or a metabolite such as the phenol content of urine used as a monitor of benzene exposure. While breath sampling is the least invasive, it may not be the best estimate of exposure over a period of time, and is often the most variable. Urinary analysis is also quite variable, and correction for concentration is often made using the analysis of the creatinine component. Blood is the most difficult fluid to take on a

Table 1 Organic chemicals with biological exposure indices

Chemical	*Measured marker*
Organic chemicals monitored in urine	
Acetone	Acetone
Aniline	*p*-Aminophenol
Benzene	*s*-Phenylmercapturic acid
Carbon disulfide	2-Thiothiazolidine-4-carboxylic acid
Chlorobenzene	4-Chlorocatechol or *p*-Chlorophenol
N,N-Dimethylacetamide	*N*-Methylacetamide
N,N-Dimethylformamide	*N*-Methylformamide
2-Ethoxyethanol and 2-ethoxyethyl acetate	2-Ethoxyacetic acid
Ethyl benzene	Mandelic acid
Furfural	Furoic acid
n-Hexane	2,5-Hexanedione
Methanol	Methanol
2-Methoxyethanol and 2-methoxyethyl acetate	2-Methoxyacetic acid
1,1,1-trichloroethane	Trichloroacetic acid or trichloroethanol
4,4′-Methylene bis(2-chloroaniline) (MBOCA)	MBOCA
Methyl ethyl ketone	Methyl ethyl ketone
Methyl isobutyl ketone	Methyl isobutyl ketone
Nitrobenzene	*p*-Nitrophenol
Parathion	*p*-Nitrophenol
Pentachlorophenol	Pentachlorophenol
Perchloroethylene	Trichloroacetic acid
Phenol	Phenol
Styrene	Mandelic acid or phenylglyoxylic acid
Tetrahydrofuran	Tetrahydrofuran[a]
Toluene	Hippuric acid or *o*-cresol[a]
Trichloroethylene	Trichloroacetic acid or trichloroethanol
Xylenes	Methylhippuric acid
Organic chemicals monitored in blood (venous unless otherwise specified)	
1,1,1-trichloroethane	Trichloroethanol
Pentachlorophenol	Pentachlorophenol (in plasma)
Perchloroethylene	Perchloroethylene
Styrene	Styrene
Toluene	Toluene
Trichloroethylene	Trichloroethylene or trichloroethanol
Organic chemical measured in breath (end exhaled air)	
Ethyl benzene	Ethyl benzene
n-Hexane	*n*-Hexane
1,1,1-trichloroethane	1,1,1-trichloroethane
Perchloroethylene	Perchloroethylene
Trichloroethylene	Trichloroethylene

[a]Notice of intended change (1998).
1998 Threshold Limit Value (TLVs®) and Biological Elxposure Indices (BEIs®) book.
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regular basis, but it is used, for example, in the regulation of exposure to lead. The American Conference of Governmental Hygienists (ACGIH®) TLV booklet also includes a listing of Biological Exposure Indices (BEI®s). A list of current BEIs and the marker compounds is given in **Table 1**.

Breath samples may be collected in special containers, or passed through sorbent tubes to concentrate the chemicals of interest. The sample can then be introduced into a gas chromatograph using a gas-sampling loop, or through solvent or thermal desorption of the sorbent. The humidity of the exhaled breath is an interfering factor, as is also the presence of chemicals manufactured by normal biological processes within the body. Blood and urine samples are more difficult to analyse chromatographically because of the matrix. Urine samples can be injected into a GC if the injection liner is replaced frequently, but blood contains surfactants and is a much more difficult medium. Liquid–liquid or liquid–solid

extraction, static and dynamic head space analysis, or solid-phase microextraction have all been used as sample preparation techniques. Many metabolites are highly polar, water-soluble compounds and HPLC is often the preferred analytical technique, especially where the presence of aromatic rings allows ultraviolet detectors to be used. However, many of the compounds listed can be analysed by GC as they are, or after derivatization. The final choice of method may depend on a number of factors.

Special care must be taken in the timing of the sample in relation to the work-periods, and also in the taking of the sample. For example breath samples should be of end-exhaled air, and blood samples should be of venous rather than capillary blood. In addition, some standards are based on total urinary excretion and others on urinary concentration. The sample container and the presence of sample preservatives are also important.

Sources of Methods

The US National Institute for Occupational Safety and Health (NIOSH) has been responsible for the *NIOSH Manual of Analytical Methods* (NMAM), now in its fourth edition. The NMAM is the largest repository of methods in the world, and many of its methods have been adopted by government agencies in other countries, such as the Health and Safety Laboratory of the UK. **Table 2** gives a list of commonly used NIOSH methods together with the chromatographic columns used (most methods use carbon disulfide, sometimes with a polar modifier, as the desorbing solution and flame ionization detection).

Validation of Methods

The validation of methods should encompass all stages of the method, including both the sampling and analysis steps. The NMAM contains details of the NIOSH method validation objectives, and a detailed validation manual for pumped sampling methods has been published (see Further Reading section). In addition, the NIOSH has supported the ASTM Standard D6246 for evaluating the performance of diffusive samplers. The US Occupational Safety and Health Administration (OSHA) Methods Manual contains similar documentation. The UK Health and Safety Executive also has standard method validation protocols (e.g. MDHS 27 for diffusive samplers). **Table 3** lists the American Society for Testing and Materials (ASTM) standards covering the analysis of air samples.

Sorbent Selection for Air Sampling Methods

The choice of chromatographic analysis procedure is intimately associated with the selection of the sorbent and the desorption procedure. Both the column type and the detector possibilities depend on the type of sample finally presented for analysis. While published methods give guidance, experienced analysts can develop or modify procedures to meet most eventualities. For example, the analysis of benzene may vary depending on whether benzene has been collected as part of a simple or complex mixture, and whether it is necessary to quantify only the benzene or all components, whether the sample was collected on charcoal or a polymer sorbent, whether the desorption is with a simple solvent or a mixture or by heat, and whether detection is by flame ionization (FID), photoionization (PID) or mass spectrometry (MS).

Charcoal is the most widely used sorbent for organic vapours. Various sources of charcoal are used, but in all cases the porosity has been enhanced by activation. Charcoals normally require solvent desorption. Anasorb® 747 is a popular charcoal from petroleum precursors that has wide application in the OSHA methods. Ambersorb®s are charcoals derived from controlled carbonization of organic polymers.

Porous polymers include cross-linked styrene and divinyl benzenes, which can have relatively large pores (Chromosorb 102, Amberlite XAD-2) or smaller micropores (Chromosorb 106, Porapak or Hayesep Q, Amberlite XAD-4). Also used are polar sorbents derived from acrylonitrile (Chromosorb 104, Amberlite XAD-7) or pyrrolidones (Porapak N, R). Tenax has a very small surface area and is normally only used for sampling low concentrations. It has the advantage of having a very low adsorption capacity for water. Because of its higher surface area and adsorption capacity, hydrophobicity, and compatibility with both solvent desorption and thermal desorption, Chromosorb 106 has been generally regarded as the most suitable polymer for occupational hygiene sampling. However, if thermal desorption is used the upper temperature limit of Chromosorb 106 is only 250°C, compared with 350°C for Tenax or Carbotrap® (a graphitized carbon), rendering it unsuitable for the collection of semi-volatile components. Styrene polymers such as chromosorb 106 also tend to have significant background when used for thermal desorption of the low concentrations found in ambient or residential indoor air, so that Tenax or Carbotrap are better.

The graphitized carbons mentioned above are available in different surface areas (e.g. Carbotrap C is approximately 10 $m^2 g^{-1}$ and Carbotrap B is

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Table 2 Methods from the *NIOSH Manual of Analytical Methods* (all columns are 3.2 mm i.d. × 3 m packed columns unless otherwise specificed)

Method name	*Method no.*	*Column used*	*Alternatives*
Hydrocarbons BP 36–126°C	1500	20% SP-2100	
Benzene			50/80 mesh Porapak P
Cyclohexane			50/80 mesh Porapak Q
Cyclohexene			50/80 mesh Porapak Q
n-Heptane			10% OV-101
n-Hexane			10% FFAP
Methylcyclohexane			10% FFAP
n-Octane			10% FFAP
n-Pentane			10% FFAP
Toluene			50/80 mesh Porapak Q
Hydrocarbons aromatic	1501	10% OV-275	
Benzene			50/80 mesh Porapak P
p-*t*-Butyltoluene			10% FFAP
Cumene			10% FFAP
Ethylbenzene			10% FFAP
α-Methylstyrene			10% FFAP
Naphthalene			10% OV-101
Styrene			10% FFAP
Toluene			50/80 mesh Porapak Q
Vinyltoluene (*o*, *m* and *p*)			10% FFAP
Xylene (*o*, *m* and *p*)			50/80 mesh Porapak Q
Hydrocarbons halogenated	1003		
Benzyl chloride		10% SP-1000	
Bromoform		10% SP-1000	
Carbon tetrachloride		10% SP-1000[a]	
Chlorobenzene		10% SP-1000	
Chlorobromomethane		10% SP-1000	
Chloroform		10% SP-1000[a]	
o-Dichlorobenzene		10% OV-101	
p-Dichlorobenzene		10% SP-1000	
1,1-Dichloroethane		10% SP-1000	
1,2-Dichloroethylene		10% SP-1000	
Ethylene dichloride		10% OV-101	
Hexachloroethane		3 m × 6 mm o.d. glass, 3% SP-2250	
1,1,1-Trichloroethane		10% OV-101	
Tetrachloroethylene		10% OV-101	
1,1,2-Trichloroethane		10% OV-101	
1,2,3-Trichloropropane		10% FFAP	
			SP-2100
			SP-2100 0.1% Carbowax
			DB-1 capillary
Naphthas	1550	10% SP-2100	DB-1 capillary
Petroleum ether			
Rubber solvent			
Petroleum naphtha			
VM&P naphtha			
Mineral spirits			
Stoddard solvent			
Kerosene			
Coal tar naphtha			
Esters 1	1450	5% FFAP	10% SP-1000
n-Amyl acetate			
sec-Amyl acetate			
n-Butyl acetate			
sec-Butyl acetate			
t-Butyl acetate			
2-Ethoxyethyl acetate			
Ethyl acrylate			

Table 2 *Continued*

Method name	*Method no.*	*Column used*	*Alternatives*
Isoamyl acetate Isobutyl acetate Methyl isoamyl acetate *n*-Propyl acetate			
Ketones 1 Acetone Cyclohexanone Diisobutyl ketone 2-Hexanone Methyl isobutyl ketone 2-Pentanone	1300	Glass, 3.5 m × 6 mm i.d. 10% SP-2100 0.1% Carbowax	10% SP-2100 or DB-1 capillary
Alcohols 1 Ethanol Isopropyl alcohol *t*-Butyl alcohol	1400	Glass, 2 m × 4 mm i.d. 0.2% Carbowax	10% FFAP
Alcohols 2 *n*-Butyl alcohol *sec*-Butyl alcohol Isobutyl alcohol *n*-Propyl alcohol	1401	Glass, 3 m × 2 mm i.d. 10% SP-1000	10% FFAP

[a]6 m column.

approximately 100 $m^2 g^{-1}$) and are used with thermal desorption in environmental applications. They have been used less often in occupational hygiene investigations, although the NIOSH has recently included a semi-quantitative screening method involving tubes containing multiple layers of sorbents including graphitized carbons in combination with carbon molecular sieves. Carbon molecular sieves, such as the Carboxen® series, can be used to sample the most volatile compounds, but have the disadvantage of also trapping large amounts of water vapour from atmospheres of high humidity.

Silica gel is a highly polar and quite strong adsorbent, useful for very polar compounds such as methanol or amines. Strong adsorption of water is a problem with using this sorbent for other chemicals. Because of this adsorption of water, silica gel is used in specific applications, such as the collection of methanol with subsequent desorption by water and analysis on a packed Tenax column with FID.

Table 3 ASTM standards (1998) covering chromatographic analysis of air samples

Standard	*Area of application*
Test methods	
D4947	Chlordane and heptachlor
D6209	Gaseous and particulate polycyclic hydrocarbons
D4413 and 5578	Ethylene oxide
D5075	Nicotine and 3-ethenylpyridine
D4766	Vinyl chloride
D5466	VOCs (canister method)
Practices	
D3686 and 3687	VOCs (charcoal tube method)
D4861	Pesticides and polychlorinated biphenyls
D6060	Sampling process vents with a portable gas chromatograph
D6196	Selection of sorbents for thermal desorption

VOC, volatile organic compound.

Solvent versus Thermal Desorption

There are significant drawbacks to the use of solvents for the recovery of chemicals from sorbent samples, not the least of which is the added hygiene and safety burden of handling a solvent such as carbon disulfide. Solvents do not always give 100% recovery, and recoveries significantly less than 75% may be associated with increased variability in the precision of recovery. It may be difficult to optimize a solvent for best recovery of a mixture of polar and nonpolar chemicals, and the solvent may interfere with chemicals in the mixture. There are special problems relating to the adsorption of water from atmospheres of high humidity, and its subsequent release from the sorbent on addition of the desorbing solvent. For

example, charcoal can absorb large quantities of water (hundreds of milligrams per gram) from atmospheres of humidity greater than 50%. This water is displaced by carbon disulfide but does not mix with it. Polar compounds such as acetone can partition into the separate water phase causing an apparent drop in recovery. Several options have been developed to deal with polar compounds, including adding a polar modifier (e.g. 2-propanol or dimethylformamide) to carbon disulfide, or switching to an altogether different solvent (e.g. 95% dichloromethane/5% methanol). However, it is difficult to substitute entirely for carbon disulfide because of its small response with the FID and its good recovery of nonpolar compounds. New carbon sorbents such as Anasorb 747 exhibit much better adsorption and desorption properties under these conditions. When using polymer sorbents, care must be taken in the choice of recovery solvent. While styrene polymers are compatible with most solvent systems, Tenax will swell in some solvents, and pyrrolidone polymers may dissolve.

An alternative to solvent desorption is thermal desorption. In this technique the sorbent tube is heated while a stream of carrier gas removes the collected vapours. Because this transfer can take several minutes the recovered vapours are usually focused in a secondary trap. There are several varieties of secondary trap in common use, including large sorbent traps at ambient temperature, open capillary tubes cooled cryogenically, and narrow-bore sorbent traps cooled to sub-ambient temperatures by Peltier cooling. The latter method provides for rapid transfer of the analytes to the column, with effective transfer of compounds in the range C_2–C_{30}, and without risk of ice blockage or condensation of permanent gases such as oxygen. Some specialized analyses of thermally labile compounds such as nerve agents or vesicants may require derivatization prior to desorption.

Thermal desorption has existed since the mid-1970s, but has not significantly replaced solvent desorption in most countries for several reasons. Efficient thermal desorption requires a sorbent with less attraction for the vapours of interest than charcoal. The use of sorbents with lower surface areas and smaller capacity can lead to premature breakthrough of the sample during the sampling period. Sorbent tubes for solvent desorption are designed with a 'back-up' sorbent section that can be analysed to detect such breakthrough but sorbent tubes for thermal desorption are not. There are also quality assurance issues that must be addressed, for example, in calibrating the analysis (standards must be added as solutions to blank tubes and then the solvent removed), using internal standards (more easily added to a solvent) or making multiple analyses (which would normally require taking multiple samples). Water management can also be a problem with thermal desorption of real-world samples. The transfer of desorbed water onto a capillary chromatographic column can alter the pressure gradient across the column and the polarity of the system, changing both retention time and peak area. Where sorbent tubes contain hydrophilic sorbents their performance can be improved by drying the sample with 300 mL of helium prior to desorption. Thermal desorption is often used for the analysis of canister samples, with the contents of the canister being drawn through the secondary trap or focusing tube, which is then desorbed and analysed. Water management may also be necessary in the analysis of canister samples. The UK Health and Safety Laboratory is the main source of published thermal desorption methods.

One important major advantage of thermal desorption is the possibility of increasing the quantity of sample that can be placed on the chromatographic column, by means of the secondary focusing trap. Recent developments in optimizing the technology now allow complete on-column injection of the entire sample, raising detection limits as much as two orders of magnitude over solvent injections. This is very useful for ambient and indoor air investigations at ppb levels, and also is making the system attractive for workplace analyses where there are chemicals with exposure limits at 1 ppm or below (e.g. benzene). When using thermal desorption for such trace analyses particular attention must be paid to the background levels of the sorbent (typically no more than 1 ng per component and 10 ng total) and handling, transport and storage procedures for the tubes. Thermal desorption also has potential applications in the analysis of biological samples, either through sorbent trapping from breath, or from direct heating of blood or urine samples. Both solvent and thermal desorption systems can be automated.

Types of Columns

When methods were being selected and validated in the early 1970s capillary chromatography was not far advanced commercially. Nor was it particularly necessary, since neither sensitivity nor selectivity was an issue. Typical occupational exposure limits at that time ranged from 10 to 1000 parts per million by volume of air for an 8-h time-weighted average. Assuming a full-shift sample using a sample tube operated at 20 mL min^{-1} (approximately 10 L of air), the tube could contain up to 10 mg of sampled chemical. Even if this were diluted in several millilitres of

solvent, a single injection into the gas chromatograph typically contained micrograms of the chemical. In addition, chemicals were less often used in complex blends, so that interfering peaks were less common. Typically, the only separation required was between the solvent, a single chemical in the sample and an internal standard. This was achieved easily with 1/8th inch (3.2 mm) packed columns, even in isothermal mode, and this procedure could be extended to cover many simple solvent mixtures used in industrial applications. A selection of the columns used in the NMAM is given in **Table 2**.

Packed columns continue to be used today for permanent gases, such as the sulfur gases (sulfur dioxide, sulfur trioxide, hydrogen sulfide, carbonyl sulfide, carbon disulfide and mercaptans), or for very volatile compounds such as 1,3-butadiene. The packings are typically zeolite or carbon molecular sieves, or, in the case of the two examples just given, alumina-PLOT columns have been used. However, as occupational exposure limits continue to fall (on average by an order of magnitude between 1980 and 1990), and the number of regulated chemicals increases and complex mixtures become more common, there is a distinct move towards the use of capillary columns, which is supported by laboratories wishing to speed up analytical procedures. This has been recognized by the NIOSH, who intend to begin a programme of updating the methods in the NMAM to include capillary columns. The typical modern occupational hygiene laboratory will have a collection of capillary columns from 15 to 100 m length, both microbore (0.32 mm) and megabore (0.53 mm), with different films and thicknesses. A standard all-purpose column might be a DB-1 or DB-5 or equivalent from other manufacturers. A typical example of a complex analysis is the determination of trace benzene (American Conference of Governmental Industrial Hygienists threshold limit value (TLV) for 1999 is 0.5 ppm) in the presence of gasoline (see **Figure 4**).

Types of Detectors

The flame ionization detector has been the traditional detector of choice in industrial hygiene analyses. It has a very wide linear range. With packed columns, limits of quantitation range typically from 2 to 20 ng of chemical per injection. The sharper peaks obtained with capillary columns can allow quantitation at lower concentrations, but this must be balanced against the smaller sample loading. Sample loading can be increased with megabore capillary columns, or by preconcentration at the injection stage. Overall limits of quantitation of 0.1–1 ng per injection are possible. Halogenated hydrocarbons do not provide as many ions in the flame and therefore have smaller detector responses. In addition, reactions with remnant ions from the carbon disulfide solvent can alter the response of halogenated hydrocarbons at low concentrations. Photoionization detectors (PIDs) are often used with portable gas chromatographs since only a single source of gas is required; however, care must be exercised in keeping the lamp clean in field use. The PID is also useful for the detection of aromatic hydrocarbons in the presence of aliphatic hydrocarbons (e.g. benzene in gasoline). The electron-capture detector (ECD) is often preferred for halogenated solvents, but the ECD is not compatible with large quantities of carbon disulfide solvent and other solvent recovery systems (e.g. hexane, ethyl acetate, toluene) do not provide as efficient recovery from charcoal sorbents.

Mass spectrometry (MS) has become popular for the analysis of trace organic components in the atmosphere through methods promulgated by the EPA. The development of quadrupole detectors has allowed the rapid scan of spectra in the timescale of a capillary peak. When the spectra are matched to a reference library, compound identification is possible, especially when this information is cross-referenced to specific compound retention times from Kováts indices. However, because MS detectors have been costly to purchase and maintain, while FIDs have had adequate sensitivity and the compounds of interest are known in advance, MS methods have not been developed for occupational hygiene analyses. This is changing and a recent example from the NMAM (method 2539) is a screening method for aldehydes (**Figures 5** and **6**). In investigations of the quality of ambient or indoor air, the dilution of the sample by solvent desorption effectively puts most contaminants below the limits of quantitation of both the FID and MS. The mass spectrometer therefore is most suitable in combination with thermal desorption for sampling multiple unknown contaminants at low concentrations. For this application a semi-quantitative NIOSH screening method (method 2549) has been developed. MS in single-ion mode can increase detection limits by a factor of 10 or more. Two examples are given showing the usefulness of the MS detector in compound identification and quantitation. Both involve the analysis of benzene in complex samples. In Figure 4 the single peak at the retention time of benzene is resolved in the MS scan as a mixture of benzene and another compound (possibly cyclohexane). In **Figure 7** the single peak is resolved into benzene and butanol. In both cases benzene could be quantified at low concentrations without interference by measuring the m/z 78 ion in single ion mode.

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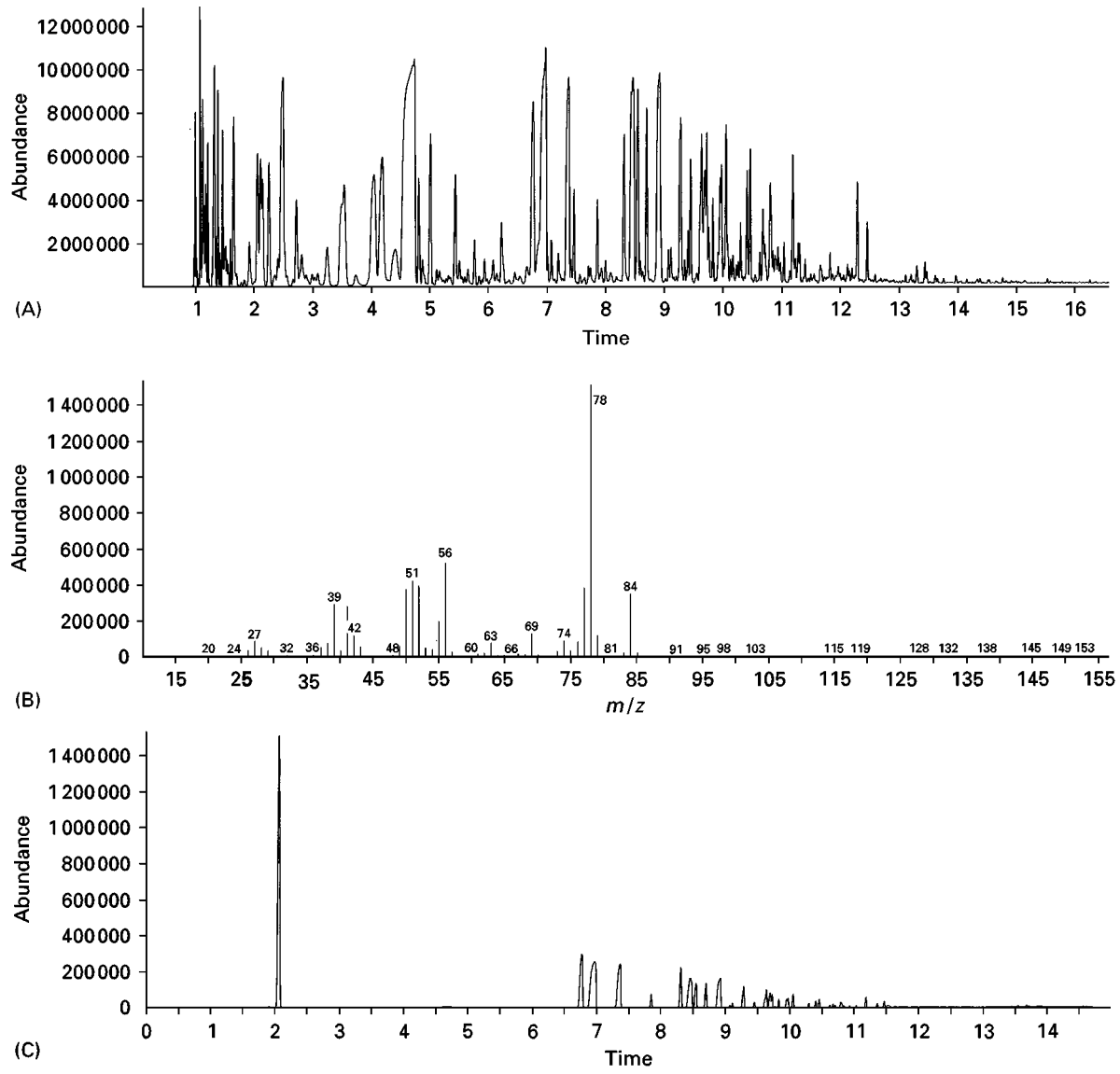

Figure 4 Determination of benzene in gasoline using GC-MS. The GC column was a 5% phenylmethylsiloxane HP-5MS. (A) Total ion chromatogram (note an FID trace would be similar). Retention time of benzene is 2.06 min. (B) Mass spectrum of peak at 2.06 min resolves interference from a C_6H_{12} compound. (C) Single ion scan at *m/z* 78 can be used to quantify benzene.

Other alternatives to the FID are normally used in trace-level compound-specific analyses, and detection limits may be enhanced by derivatization. For example, formaldehyde may be determined as a derivative with hydroxymethylpiperidine using a nitrogen–phosphorous detector. Sulfur compounds are often detected using a flame photometric detector (FPD).

Quality Assurance

The number of samples taken per investigation will depend on the number of exposed workers and the perceived extent of any problem and may vary from one to several hundred. The best choice of laboratory for analysing occupational hygiene samples is one that specializes in such samples and accepts them on a routine basis. Laboratories may voluntarily participate in Proficiency Analytical Testing (PAT) schemes or, once they have established proficiency in these schemes, request accreditation by various recognized bodies. In the USA the proficiency samples for organic solvents include aliphatic, aromatic and chlorinated hydrocarbons, alcohols, ketones and esters. Many other countries have similar proficiency testing and accreditation programmes. For example, the UK Health and Safety Laboratory operates the Workplace Analysis Scheme for Proficiency (WASP).

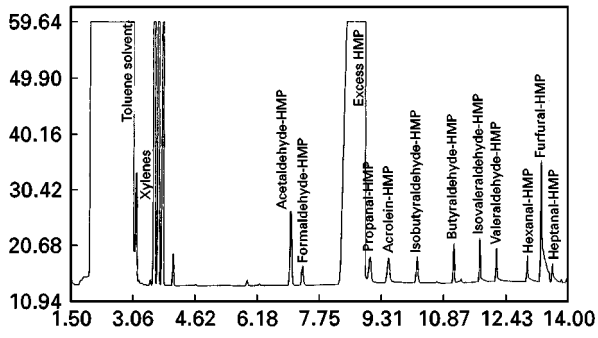

Figure 5 Determination of multiple aldehydes as their derivatives with 2-hydroxymethylpiperidine. Total ion chromatogram of aldehyde mix from spiked sorbent tube separated on a 15 m DB-1301 column.

In addition to documentation of methods and practices, the following specific elements are considered appropriate for good analytical practice:

- *Initial calibration verification*. This is based on a range of standards diluted from a stock solution. Multiple points encompassing the expected sample range are used to create a calibration curve. If the samples fall outside this range, further standards are prepared. The response of the detector to the standards, and their correlation coefficient, should be within control limits. Field-portable detectors may use packaged calibration gases.
- *Continuing calibration verification*. At least one of the standards used for the initial calibration is repeated each 10–20 injections (or more frequently if considered desirable).
- *Internal standards*. An internal standard is useful to compensate for minor variations in the sample size injected into the GC, but because it may mask a chemical of interest internal standards are not always employed where the sample is not well characterized.
- *Reagent blanks*. The solvent used to make up standards and desorb samples is checked for contamination. This procedure is essential if low concentrations of analyte are to be determined.
- *Matrix blanks*. The sampling medium is checked for contamination.
- *Matrix spikes*. A known quantity of the analyte is added to a blank sample medium, which is carried through the full analytical procedure to ensure proper recovery.
- *Replicates*. Used to ensure the precision of analysis. Particularly useful at low sample concentrations.
- *External standards*. Known concentrations of the chemical of interest obtained from a source other than the laboratory. Standard mixtures of commonly analysed chemicals are obtainable from speciality sources.

Other quality assurance methods used less often include: using a surrogate (a compound that behaves similarly to that of interest, but which can be separated, such as a deuterated analogue, which is used in the same way as a matrix spike with actual samples), matrix additions (direct addition of known quantities of the chemical of interest, which are subtracted from the final result) and splitting the sample (division of the sample for separate analyses).

Portable Gas Chromatographs

The detectors used in GC, especially the FID and the PID, are often used as stand-alone instruments for 'total' hydrocarbon analysis. They are calibrated to a standard concentration of an alkane in air. These detectors may also be used with a portable gas chromatograph to transfer laboratory analytical techniques to the field. Time-integrated samples can be collected using a sampling bag and are introduced using a gas-tight syringe. Built-in sampling pumps can give semi-'real time' measurements. Some instruments operate at ambient temperatures, but are limited to gases and very volatile compounds; most have some capability for temperature programming. Both packed and capillary column instruments are available, but since their introduction in the early 1980s wide-bore capillary columns have become standard. A detection limit of 0.1 ppb is claimed by one manufacturer (probably for an ECD), but most are higher, up to 0.1 ppm using PIDs or FIDs. Some are available with an option for different detector or injector types. Most can be linked to a personal computer. Many are mains powered but some use rechargeable batteries with a life of around 8 h or better. All are relatively heavy (< 20 kg), and none are truly considered 'personal' samplers. There are significant issues of user training and field calibration, and compressed gases (for carrier gas or instrument calibration) and radioactive sources (e.g. ECDs) cannot be transported on commercial aircraft. A very recently developed instrument uses ambient air as the carrier gas. While detection limits and separations are not as good as with helium, no compressed gases are required for instrument operation if the detector is a PID, or an FID with hydrogen generated by electrolysis of water.

To date, portable gas chromatographs have not been used for compliance monitoring by the OSHA, nor have they replaced traditional personal sampling methods, although the NIOSH has developed several analytical methods that use a portable gas chromatographs for analysis of exhaled breath, or

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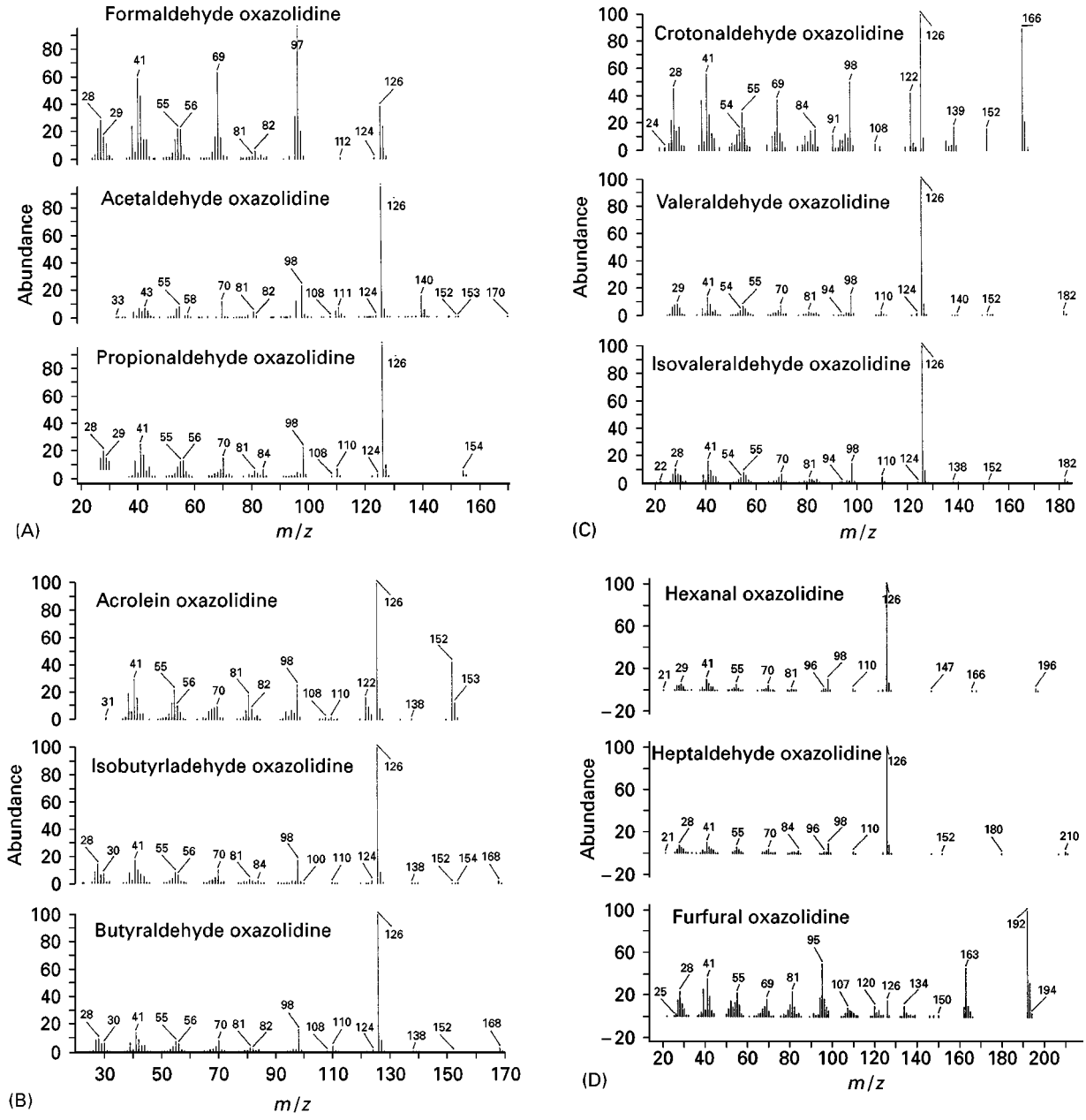

Figure 6 Determination of multiple aldehydes as their derivatives with 2-hydroxymethylpiperidine. Individual reference spectra using a 70 eV HP 5970 mass selective detector at 20–400 a.m.u. scan (30 m DB-1 column).

polluted air, or in ventilation studies (3700 for benzene, 3702 for ethylene oxide and 3701 for trichloroethylene using a PID, 6603 for carbon dioxide (TCD) and 6602 for sulfur hexafluoride (ECD)). In all cases these methods require samples to be collected in bags before analysis. Portable gas chromatographs have the advantage of near real-time response, which can be combined with observation of the work activity, for example by video monitoring, to gauge the effect of different work practices and control measures. Other applications include exhaled breath analysis, measuring the penetration of organic chemicals through protective clothing, providing assurance of safe entry into confined spaces, and monitoring at hazardous waste sites and spills.

The Future

Traditional occupational hygiene sampling and analysis is already facing problems with sensitivity. As an example one can cite the NIOSH method for acrylonitrile. The NIOSH recommended exposure

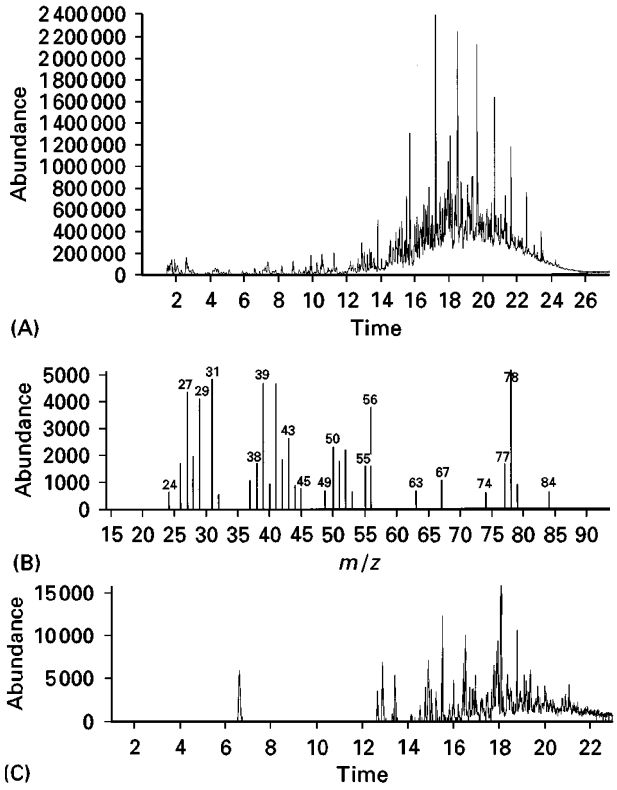

Figure 7 Air sample taken during asphalt paving operations analysed by TD-GC-MS (30 m DB-1 column). (A) Total ion chromatogram. Retention time of benzene is 6.6 min. (B) Mass spectrum of peak at 6.6 min showing the presence of butanal in addition to benzene. (C) Single ion chromatogram of *m/z* 78 benzene ion, eliminating other hydrocarbon interferences.

limit is 1 ppm, but the lower limit of the method is only slightly less at 0.7 ppm. Several other chemicals (e.g. benzene, 1,3-butadiene, vinyl chloride, ethylene oxide, etc.) have exposure limits close to the lower limit of their method range. In almost no case has an exposure limit been raised – the limit for benzene fell from 100 ppm (1946) to 25 ppm (1961) to 10 ppm (1978), and the current Threshold Limit Value® (TLV) is 0.5 ppm. Clearly the challenge is to find more sensitive methods of detection. One route is to use capillary chromatography, another is to use thermal desorption, and another is to use MS detection. The combination of all three can yield a sensitivity of around 0.1 ng per sample (equivalent to 0.03 μg m^{-3}, or 0.1 ppb, for a 3-L sample). One problem with such a combination is the cost, which can be as much as ten times that of the analysis of a conventional charcoal tube by solvent desorption and GC-FID. The advent of fast GC systems may lower the cost by allowing a greater daily sample throughput.

Another issue for the field is the long turn-around time for the result (sometimes weeks). Detectors that can give on-site results are clearly preferable. With micro-miniaturization (the 'GC-on-a-chip') this may become achievable in the near future.

Acknowledgements

The author is indebted to Dr Eugene Kennedy and Dr Ardith Grote (NIOSH, Cincinnati, OH, USA) for the use of Figures 4–7.

See also: **II/Chromatography: Gas:** Detectors: Mass Spectrometry; Detectors: Selective; Gas Chromatography-infrared; Headspace Gas Chromatography; Multidimensional Gas Chromatography; Sampling Systems. **III/Solid-Phase Microextraction:** Environmental Applications; Overview.

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